

SUPPORT FOR THE AMENDMENTS

Claims 3 and 8 were previously canceled.

Claims 1, 2, 4, and 7 have been amended.

The amendment of Claims 1, 2, 4, and 7 is supported by the corresponding previously pending claims and the original specification as filed, for example at page 1, line 10 to page 2, line 8, page 12, line 16 to page 13, line 4, page 16, line 24 to page 17, line 11, and the Examples.

No new matter has been entered by the present amendment.

REMARKS

Claims 1, 2, 4-7, 9, and 10 are pending in the present application.

The rejection of Claims 1, 2, 4, and 7 under 35 U.S.C. §112, first paragraph (enablement), is obviated in part by amendment and traversed in part.

The Office has taken the position that the claimed invention is not supported by an enabling disclosure. Applicants respectfully disagree.

Applicants remind the Examiner of MPEP § 2164.01, which states:

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.

Applicants submit that practicing the claimed invention would not require experimentation that would be considered to be “undue”.

In making this rejection, the Examiner raises several points of criticism. For sake of convenience, each of these issues is addressed below along with Applicants comments:

- 1) The Examiner alleges that the argument at page 7 of the response filed on May 7, 2007, provides unsubstantiated statistics. Specifically, the argument the Examiner criticizes is:

”In attempting to provide summaries as to the state of the art, the Examiner cites four U.S. pre-grant publications. However, what the Examiner overlooks in this citation is their relevance, or lack thereof, to the claimed invention. Specifically, it is noted that the genome of yeast is approximately  $1.25 \times 10^7$  bp. Therefore, the minimal polynucleotide sequence that can be considered to be a statistically unique sequence in the yeast genome is a twelve-mer. The probability of a twelve-mer being randomly repeated is calculated as  $4^{12}$ . Thus, the corresponding frequency is one occurrence every  $1.7 \times 10^7$  bp. In Claim 1, the first primer is SEQ ID NO: 7 (i.e., a 20-mer with an estimated frequency of once every  $1.0 \times 10^{12}$  bp), while the second primer in the pair ranges from 15 (estimated frequency of once every  $1.0 \times 10^9$  bp) to 30 (estimated frequency of once every  $1.0 \times 10^{18}$  bp) nucleotides. In Claim 2, the first primer is defined as SEQ ID NO: 7 and the second primer is defined as SEQ ID NO: 8 (both 20-mers with an estimated frequency of once every  $1.0 \times 10^{12}$  bp). In view of the foregoing, Applicants submit that the primers of the present invention represent statistically unique sequences on the yeast genome and, thus, improper or false

priming is of no relevance.”

The Examiner’s allegation that these statistics are unsubstantiated appears to be a misunderstanding of the basic principles of DNA technology. As is well-known in the art, the frequency of any specific sequence of “n” length is determined as  $4^n$ , which is the mathematical expression of “for each position in the polynucleotide there are four choices of nucleotides. Therefore, if there are “n” positions each of which has four choices, the number of sequence variants over the “n” positions is  $4^n$ .”). Further with respect to the genome size for yeast, the Examiner is referred to any genome database including: <http://www.ncbi.nlm.nih.gov/genomes/leuks.cgi>, which evidences that the number of nucleotides in yeast (i.e., *Saccharomyces cerevisiae*) publicly known at the time of the present invention.

In view of the foregoing, this ground of rejection is without merit and should be withdrawn.

- 2) The Examiner asserts that the arguments as to the lack of false priming due to the “uniqueness” of the primers is not persuasive because the method is not limited to any specific PCR conditions and the specification fails to “teach how the inherent error rate of the polymerase is to be overcome, when as here, there is no upper limit to the number of cycles of amplification to be practiced.” We continue to disagree and submit that PCR conditions would be well known to the skilled artisan and would not amount to undue experimentation, which is further underscored by the disclosure at page 12, line 16 to page 13, line 4, page 16, line 24 to page 17, line 11, and the Examples.

Despite the foregoing, Applicants have amended the claims to define the PCR conditions based on page 12, line 16 to page 13, line 4, page 16, line 24 to page 17, line 11, and the Examples as follows: denaturing for 10 seconds to 2 minutes at a temperature of 90-98°C, annealing for 20 seconds to 2 minutes at a temperature of 40-75°C, and extending for 1-20 minutes at a temperature of 65-75°C, with 10-30 cycles.

In view of the foregoing, Applicants submit that this ground of rejection should be withdrawn.

- 3) The Examiner further alleges that the primers appearing in the claims are not actually limited to the recited sequences. As indicated above in regard to the anticipation rejection, the Examiner interprets “comprising” a recited sequence as embracing “fragments thereof, and primers that have mutations, substitutions, rearrangements, etc.”. Even though Applicants disagree they have amended the claims to replace “comprising” with “consisting of” when defining primers (i) and (ii).

In view of the foregoing, Applicants submit that this ground of rejection should be withdrawn.

- 4) Finally, the Examiner alleges that “there is nothing that precludes other primers from being present. Indeed, the claimed method fairly encompasses performing multiplex PCR. Clearly, the specification is silent as to what reagents and conditions are to be

employed when such an embodiment is to be performed.” There is good reason why the specification is silent as to reagents and conditions... the claims and the specification do not embrace or contemplate multiplex PCR. Nonetheless, to expedite examination, Applicants have amended the claims to further define the PCR step as follows, which also includes the amendment appearing in (2) above:

”performing PCR (Polymerase Chain Reaction) using said pair of primers and a DNA separated from a yeast specimen to produce a PCR amplification product, wherein the primers for said PCR consist of said pair of primers, the template for said PCR is a DNA separated from a yeast specimen, and said PCR is performed by denaturing for 10 seconds to 2 minutes at a temperature of 90-98°C, annealing for 20 seconds to 2 minutes at a temperature of 40-75°C, and extending for 1-20 minutes at a temperature of 65-75°C, with 10-30 cycles;”

Applicants submit that, with the present specification in hand, discrimination between bottom-fermenting yeast and wild yeast would require nothing more than routine experimentation. As such, Applicants submit that Claims 1, 2, 4, and 7 are fully enabled within the context of 35 U.S.C. §112, first paragraph.

Withdrawal of this ground of rejection is requested.

The rejection of Claim 7 under 35 U.S.C. §102(b) over New England Biolabs 2000 catalog is obviated by amendment.

The Examiner alleges that Claim 7 is anticipated by the NEB 2000 catalog. The basis for this rejection is the Examiner’s interpretation of “comprising” a recited sequence as embracing “fragments thereof, and primers that have mutations, substations, rearrangements, etc.” Applicants disagree with this interpretation. However, to expedite examination of this application, Claim 7 has been amended as follows: “A pair of primers consisting of (i) a primer ~~comprising~~ consisting of the base sequence set forth in SEQ ID NO: 7 and (ii) a primer ~~comprising~~ consisting of the base sequence set forth in SEQ ID NO: 8.”

In view of this amendment, Applicants request withdrawal of this ground of rejection. An action to the effect is requested.

The rejection of Claims 1-3 under 35 U.S.C. §112, second paragraph, is obviated by amendment.

The Examiner has held the claims to be indefinite. Specifically, the Examiner is asserting a literal interpretation of “wild yeast” and “bottom-fermenters” to embrace more than that which is defined on pages 1-2 of the specification. Applicants disagree and remind the Examiner that they can be their own lexicographer and that the specification as filed clearly defines the meaning of the objected to terms. Nonetheless, Applicants have amended the claims to define the “wild yeast” as being “wild yeast not used for brewing and being obtained from the genus *Hansenula*, the genus *Brettanomyces*, the genus *Candida*, and the genus *Saccharomyces*, wherein when the wild yeast is from the genus *Saccharomyces* said wild yeast is a species selected from the group consisting of *Saccharomyces cerevisiae*, *Saccharomyces bayanus* and *Saccharomyces diastaticus*” and the “bottom-fermenters” as being “*Saccharomyces pastorianus*”. Accordingly, Applicants submit that this ground of rejection is now moot.

Withdrawal of this ground of rejection is requested.

Applicants submit that the present application is now in condition for allowance. Early notification of such action is earnestly solicited.

Respectfully submitted,

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